UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/360,242	07/22/1999	JOHN R. MCDONALD	25020-601B	3887

7590 04/09/2002

STEPHANIE SEIDMAN
HELLER EHRMAN WHITE & MCAULIFFE
4350 LA JOLLA VILLAGE DRIVE
SAN DEIGO, CA 92122-1246

EXAMINER
LANDSMAN, ROBERT S

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 04/09/2002

32

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/360,242	MCDONALD ET AL.	
	Examiner	Art Unit	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-29,31,32,34-38,40,42,44-46,48-54,57 and 65-87* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-29,31,32,34-38,40,42,44-46,48-54,57 and 65-87* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *31* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Formal Matters

A. The Information Disclosure Statement, filed 1/17/02, has been entered into the record.

B. The Request for Reconsideration, filed 1/23/02, has been entered into the record.

C. Claims 26-29, 31, 32, 34-38, 40, 42, 44-46, 48-54, 57 and 65-87 are pending in this application.

D. All Statutes under 35 USC not found in this Office Action can be found, cited in full, in a previous Office Action.

2. Claim Rejections - 35 USC § 103

A. The previous rejection of all claims under 35 USC 103 has been withdrawn in view of the rejection below under 35 USC 102.

3. Claim Rejections - 35 USC § 112, first paragraph – scope of enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 26-29, 31, 32, 34-38, 40, 42, 44-46, 48-54, 57 and 65-87 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing cytotoxicity by contacting cells with a chemokine-toxin conjugate in vitro, does not reasonably provide enablement for a method of treating a pathological condition by administering a chemokine-toxin conjugate in vivo. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, Applicants have only provided guidance and working examples of the in vitro bioactivity of one chemokine-toxin fusion protein using an RIP assay (Example 2, page 166 of the specification). While this conjugate did inhibit protein synthesis in vitro, Applicants have not demonstrated that this, or any

chemokine-toxin conjugate, is effective in inhibiting activation, proliferation, or migration of immune effector cells in vivo. No nexus has been presented in the specification or claims as to how the inhibition of protein synthesis by inhibiting translation of luciferase RNA can be predictable of in vivo effects on a T-cell population, especially given the teaching of Volk et al. that an in vivo response to a cytokine-toxin conjugate is unpredictable based on in vitro results (page 2504, first full paragraph). Volk et al. state that even though IL-2-PE40 improve the immunosupressive efficacy of the cell-mediated immune response, there is still an undesirable humoral response. Since chemokines are considered cytokines, the same unpredictability as to the in vivo response of a chemokine-toxin conjugate based on in vitro results would be expected. Therefore, it would not be predictable to one of ordinary skill in the art how use the chemokine-toxin conjugates to treat the claimed pathological conditions in vivo.

In addition, Applicants have brought to the Examiner's attention on page 10 of the response dated 1/23/02 that the arguments regarding "Bexxar" and "Genimmune" (discussed on page 15 (Table 3) of Applicants' response dated 6/25/01) are to demonstrate operativeness and to evidence confirmation of what is taught in the instant specfication. However, as stated by Applicants, these conjugates have not received FDA approval and, therefore, the effectiveness of these compounds and their use in treating immune diseases has not yet been established.

Therefore, in summary, due to the lack of guidance and working examples of the use of chemokine-toxin conjugate to inhibit activation, proliferation, or migration of immune effector cells in vivo, as well as the unpredictability to one of ordinary skill in the art how use the chemokine-toxin conjugates to treat the claimed pathological conditions in vivo, especially given the prior teachings in the art, leads the Examiner to conclude that undue experimentation is necessary to practice the invention as claimed.

4. Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

A. Claims 35, 36, 38, 72-80, 84, 86 and 87 rejected under 35 U.S.C. 102(b) as being anticipated by Volk et al. (Reference "X" on the Form PTO-892 of Paper No. 10). The claims recite a method of targeted delivery of an agent into cells that express chemokine receptors by associating the agent with a

targeting agent wherein the immune effector cells are activated leukocytes. The claims also recite a method of inhibiting proliferation, migration, or activation of cells bearing chemokine receptors. These claims read on in vitro administration of chemokine-toxin conjugates.

Volk et al. teach the use of cytokine-toxin conjugate (IL-2-PE40) to study the effects of these compounds in mice (at least paragraphs 2 and 3 of "Results" and Table I). Volk et al. also teach that these conjugates prevent the activation of a cell-mediated response. Though Volk et al. do not specifically recite the use of chemokines, chemokines are characterized as being part of the cytokine "family" (Callard et al. - reference C on the IDS submitted 7/17/01). The Callard et al. reference is not being cited as new prior art in this rejection under 35 USC 102. It is only being cited to demonstrate and support the fact that the chemokines of the present invention are in the same family as the cytokines of Volk et al. Therefore, Volk et al. do meet the limitations of a method of targeting cells using a chemokine-toxin conjugate since cytokines, which are in the same family as chemokines, were already in use as conjugates with toxins to target immune cells. IL-2 receptors are well-known in the art to be expressed on various immune effector cells. Therefore, the use of this conjugate in mice would inherently be inhibiting either activation, proliferation, or migration of immune cells, including activated leukocytes, since the study by Volk et al. was to determine the effects of IL-2-PE40 on SRBC-challenged mice (i.e. immunologically challenged mice).

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
April 08, 2002

Gary L. Kunz

GARY L. KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600